5-AMINOLEVULINIC ACID AND HEXYL AMINOLEVULINATE MEDIATED PHOTODYNAMIC DIAGNOSTICS AND THERAPY OF CERVICAL DYSPLASIA AND VULVAR LEUKOPLAKIA

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timely diagnosis and adequate therapy for cervical dysplasia and vulvar leukoplakia can reduce the risk of developing cancer

The risk of developing cervical cancer in women with CIN is 20 times higher than that of healthy people, which is the 2nd most important type of cancer from which women die [1].

Vulvar leukoplakia progresses to cancer in 2-6% of cases [2].


The proportion of cases of cervical and vulvar cancer among women of all ages by 2020 in Russia of the total number in Europe (5 years) - WHO
comparative analysis of the use of drugs based on 5-ALA and HAL for PD and PDT of cervical dysplasia and vulvar leukoplakia

5-ALA - Alasens ®
HAL - Hexasens ®

• 5-ALA is a hydrophilic molecule (penetration through intact epithelium or cell membranes is difficult) [1].
• HAL has increased lipophilicity (better diffusing properties) [2].

5-ALA and HAL are compounds producing PpIX, which has fluorescent properties.
The application method of administration of 5-ALA and HAL was used

- The concentration of PS in solution is 10 mg/ml. The volume of the solution is 3 ml.
- PS exposure time - 2 hours.
- Patients:
  - 5 with vulvar leukoplakia
  - 2 with cervical dysplasia (CIN III)
I - after PD, a sterile dressing with a PS solution was applied to the cervix;

II - after 2 hours, PD was performed to identify foci of PpIX accumulation;

III - further PDT was performed for the foci of PpIX accumulation;

IV - after PDT, PD was performed to assess photobleaching PpIX.
PD made it possible to identify foci of PpIX accumulation and to estimate the distribution of its intensity

Photographic products are more photostable than PpIX [1].

Being more water-soluble than PpIX, photoproducts easily migrate to other intracellular microenvironment [2]

Fluorescence spectra:
a - patient with 5-ALA, b - patient with HAL


PD made it possible to identify foci of PpIX accumulation and to estimate the distribution of its intensity.
impulse action on the PpIX accumulation zones made it possible to shorten the duration of the PDT session and reduce pain.

Distribution of fluorescence indices before PDT, 2 hours after PS administration and after PDT

5-ALA (patient 1-2)

HAL (patient 3-5)

$E = 32 \text{ J} / \text{cm}^2$

The number of impulses per session - 30
PD of phantoms with known PpIX concentrations and imitating the optical properties of human skin made it possible to quantify the PS concentration in the studied tissues.

The maximum concentration of PpIX was observed with HAL:

- cervix dysplasia > 20 mg / kg
- vulvar leukoplakia > 15 mg / kg
the use of HAL in PD allows to achieve the greatest contrast of the pathologically altered tissue relative to the healthy one.

Cervical dysplasia:
- PpIX fluorescence intensity is 5 times higher with HAL compared to 5-ALA.
- CIN was absent 3 months after PDT.

Vulvar leukoplakia:
- There is no significant difference in PpIX fluorescence intensity between HAL and 5-ALA.
- 3 months after PDT, 2 patients with 5-ALA and HAL were prescribed a second course of PDT.